

NOVEL *KIF11* VARIANTS WITH NEW CLINICAL FEATURES: EXPANDING THE CLINICAL PHENOTYPE

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ABSTRACT

Monoallelic *KIF11* variants are associated with *Microcephaly with or without Chorioretinopathy, Lymphedema, or Impaired Intellectual Development (MCLMR)* (OMIM:152950). This study presents seven patients from two distinct families, exhibiting extreme clinical heterogeneity, along with novel clinical findings and genetic variants. Patient 1 presented with learning difficulties, epilepsy, behavioral abnormalities, and various ocular anomalies, in addition to microcephaly and facial dysmorphism. Patient 2 was prenatally diagnosed with dorsal pedal edema, which was confirmed postnatally, alongside facial dysmorphic features and the need for craniosynostosis surgery at four months. Peripheral blood samples were obtained for DNA isolation, and *Whole Exome Sequencing (WES)* was performed for molecular analysis. Whole-exome sequencing (WES) revealed a de novo heterozygous frameshift variant in the *KIF11* gene (NM_004523.4: c.2224_2225del; p. Asn742TyrfsTer6) in patient 1, and a novel heterozygous frameshift variant (NM_004523.4: c.2946dup; p. Leu983SerfsTer6) in the same gene in patient 2. Segregation analysis demonstrated that Patient 2's variant was inherited from the mother and was also present in the maternal grandmother, sister, and two aunts. Our findings highlight the broad clinical heterogeneity of MCLMR syndrome, as Patient 1 exhibited keratoconus, optic nerve hypoplasia, behavioral problems, and seizures, which are rarely reported. Additionally, Patient 2 represents the first documented patient of pre-natal lymphedema detection in MCLMR syndrome. Furthermore, craniosynostosis, identified in two patients (P2 and P5), has not been previously described, suggesting a potential novel

phenotypic feature. These findings expand the genotypic and phenotypic spectrum of *KIF11*-related disease.

Keywords: Craniosynostosis, *KIF11*, Lymphedema, Microcephaly, Novel Variants

INTRODUCTION

Microcephaly with or without Chorioretinopathy, Lymphedema, or Impaired Intellectual Development (MCLMR, OMIM:152950) is a rare autosomal dominant disorder caused by pathogenic *KIF11* variants. The condition is characterized by microcephaly, ocular anomalies (including chorioretinopathy), congenital lymphedema affecting the lower extremities, and mild to moderate intellectual disability [1-5]. Distinctive dysmorphic facial features include upward-slanting palpebral fissures, a broad nasal tip, a long philtrum with a thin upper lip, a prominent chin, and prominent ears [1-3, 6, 7].

Additional less commonly reported clinical manifestations include optic nerve abnormalities [3], amblyopia [8], microphthalmia [9], retinal detachment [3, 8], cataracts, glaucoma [3], atrial septal defect [2], seizures [3], attention deficit hyperactivity disorder (ADHD), and behavioral disturbances, indicating multisystemic involvement.

The most frequently reported clinical features in *KIF11*-associated MCLMR syndrome are congenital microcephaly of varying severity and chorioretinal abnormalities. However, incomplete penetrance and variable expressivity are well documented [2, 5, 10].

The *KIF11* gene, located on chromosome 10q23.33, encodes EG5, a mitotic kinesin motor protein essential for bipolar mitotic spindle formation and maintenance during cell division [11-13]. EG5 is a homotetrameric kinesin containing a microtubule-binding region, an ATP-binding domain with ATPase activity, and a motor domain responsible for tetramerization [14].

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As of October 19, 2024, the ClinVar database lists 140 pathogenic or likely pathogenic *KIF11* variants, including 39 nonsense, 7 missense, 72 frameshift, and 22 splice-site variants (ClinVar, <https://www.ncbi.nlm.nih.gov/clinvar/>). These variants are distributed throughout the gene.

This study presents a family with a *KIF11* variant identified in six members, including the proband, detected through prenatal diagnosis of isolated dorsal pedal edema, as well as a *de novo* variant in a separate patient exhibiting other syndromic features without lymphedema.

MATERIALS AND METHODS

Written informed consent was obtained from the probands and their families for participation in this study and genetic analysis. A clinical geneticist evaluated all probands and their families. Genomic DNA was extracted from peripheral blood using the QIAamp DNA Blood Mini QIAcube Kit (Qiagen, Hilden, Germany) following the manufacturer's protocol. Whole-exome sequencing (WES) was performed to sequence all coding regions of the human genome to 150 bp paired ends using the Illumina NovaSeq platform and the Agilent SureSelect V5 kit (Agilent, Santa Clara, CA, USA). Raw sequencing data were analyzed using the Qiagen Clinical Insight data analysis platform. Variants were classified according to the American College of Medical Genetics and Genomics (ACMG) guidelines. Candidate variants potentially explaining the observed phenotype were validated using Sanger sequencing on the ABI PRISM® 3500xL Genetic Analyzer (Applied Biosystems, Foster City, CA, USA), followed by segregation analysis in the probands and their parents.

RESULTS

Patient 1

Patient 1 is a 7-year-old female, born to non-consanguineous, healthy parents at 36 weeks of gestation due to oligohydramnios, with a birth weight of 2600 g. She has been under clinical follow-up for five years due to learning difficulties, epilepsy, and behavioral abnormalities. At two years of age, she experienced two afebrile seizures occurring six months apart. Under antiepileptic treatment, she has remained seizure-free for the past five years. Following the onset of seizures, she exhibited increased aggressive behavior, for which she underwent play therapy (Table 1). Additionally, she has received special education due to her learning difficulties.

Her medical history is notable for high-grade myopia, astigmatism, bilateral staphyloma, optic nerve hypoplasia, and keratoconus, requiring two surgical interventions (Table 1).

At 7 years and 3 months of age, her physical examination revealed a height of 123 cm (-0.66 SDS), a weight of 26 kg (0.09 SDS), and a head circumference of 47.5 cm (-3 SDS). Dysmorphological assessment identified microcephaly, sloping forehead, synophrys, bilateral esotropia, retrognathia, and fifth-finger clinodactyly (Table 1).

Systemic evaluations, including echocardiography (ECHO), electroencephalography (EEG), abdominal ultrasonography (USG), and hearing assessments, yielded normal results. Ophthalmologic examination revealed -10 diopters of myopia, -4.5 diopters of astigmatism, and bilateral keratoconus (Table 1). Orbital magnetic resonance imaging (MRI) demonstrated findings consistent with bilateral staphyloma, while brain MRI revealed optic nerve thinning and increased periorbital cerebrospinal fluid (CSF) space (Table 1). Metabolic workup and chromosomal microarray analysis were unremarkable.

Whole-exome sequencing (WES) identified a novel heterozygous frameshift variant in the *KIF11* gene, NM_004523.4: c.2224_2225del (p. Asn742TyrfsTer6). This variant is absent in population databases (gnomAD, 1000 Genomes Project, ExAC) and was classified as pathogenic according to American College of Medical Genetics and Genomics (ACMG) criteria (PVS1, PM2, PM6). Segregation analysis confirmed the *de novo* nature of the variant (Figure 3).

Patient 2–7

Patient 2: A 2-month-old male infant, born to non-consanguineous and healthy parents at 38 weeks of gestation with a birth weight of 3200 g, presented to the medical genetics' clinic for evaluation of a potential genetic etiology. Prenatal ultrasound findings had revealed bilateral dorsal pedal edema and mild polyhydramnios, prompting the referral. Non-invasive prenatal testing (NIPT) excluded common chromosomal abnormalities, including trisomy's 13, 18, 21, and sex chromosome anomalies.

Postnatally, the patient exhibited bilateral dorsal pedal edema and facial dysmorphism, leading to a presumptive diagnosis of Milroy disease (Figure 1). At four months of age, the infant underwent surgical intervention for craniosynostosis. Pedigree analysis (Figure 2) disclosed two maternal aunts with cognitive impairment, microcephaly, and visual impairments, one of whom also had a history of craniosynostosis (Table 1).

At two months of age, clinical examination revealed a height of 57 cm (-0.57 SDS), a weight of 5.5 kg (-0.22 SDS), and a head circumference of 37 cm (-2.15 SDS). Notable dysmorphological features included microcephaly, up slanting palpebral fissures, anteverted nares with a broad nasal tip, retrognathia, prominent ears, bilateral dorsal pedal edema, and hypoplastic toenails (Figure 1).

Table 1. Clinical Features of patients With KIF11 variants.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7
Nucleotide variant	c.2224_2225del	c.2946dupT	c.2946dupT	c.2946dupT	c.2946dupT	c.2946dupT	c.2946dupT
Protein alteration	p.Asn742TyrfsTer6	p.Leu983SerfsTer6	p.Leu983SerfsTer6	p.Leu983SerfsTer6	p.Leu983SerfsTer6	p.Leu983SerfsTer6	p.Leu983SerfsTer6
Inheritance	De novo	Maternal	Maternal	Maternal	Maternal	Maternal	NA
Microcephaly	(-3 SDS)	(-2.15 SDS)	(+)	(+)	(+)	(+)	(+)
Eye abnormalities	Myopia, Astigmatism, Keratoconus, Bilateral optic nerve hypoplasia, Bilateral staphyloma	(-)	Myopia	(-)	Cataract, Severe vision loss	Severe vision loss	NA
Lymphedema	(-)	Dorsal pedal lymphedema	(-)	(-)	(-)	(-)	(-)
Intellectual disability	Moderate	(-)	(-)	(-)	Severe	Severe	Mild
Seizures	Afebrile seizures	(-)	(-)	(-)	(-)	(-)	(-)
Dysmorphic findings	Sloping forehead, synophrysis, bilateral esotropia, retrognathia and clinodactyly of the fifth finger	Upslanting palpebral fissures, anteverted nares and broad nasal tip, retrognathia, prominent ears, hypoplastic toenails	NA	(-)	NA	NA	NA
Additional clinical features	Increased periorbital CSF distance on brain MRI, Tantrums	Craniosynostosis	(-)	(-)	Craniosynostosis	(-)	(-)

(NA: Not Available)

**Figure 1. Clinical Features of Patient 2.** a, b. Facial phenotype of Patient 2. Note broad nasal tip, anteverted nares, upsanting palpebral fissures, retrognathia and prominent ears. c. Lymphedema of the dorsum of the foot and hypoplastic toenails.

Despite these features, the patient's motor development was within normal limits, with walking initiated at 11 months and speech development at 12 months.

Abdominal and renal ultrasonography yielded normal results. Brain MRI showed no abnormalities, and echocardiogram (ECHO) revealed a small secundum atrial septal defect (ASD). Vision and hearing tests were unremarkable, and karyotype analysis showed a normal 46, XY pattern.

Whole exome sequencing (WES) identified a novel heterozygous frameshift variant in the *KIF11* gene,

NM_004523.4: c.2946dup (p. Leu983SerfsTer6). This variant was absent in population databases (gnomAD, 1000 Genomes Project, ExAC) and was classified as pathogenic according to the ACMG criteria (PVS1, PM2, PP1, PP4). Segregation analysis revealed the variant to be maternally inherited. Subsequent family screening identified the variant in the heterozygous state in the patient's sister, maternal grandmother, and two affected maternal aunts (Figure 2).

Clinical examination of family members carrying the variant revealed microcephaly in the mother, sister,

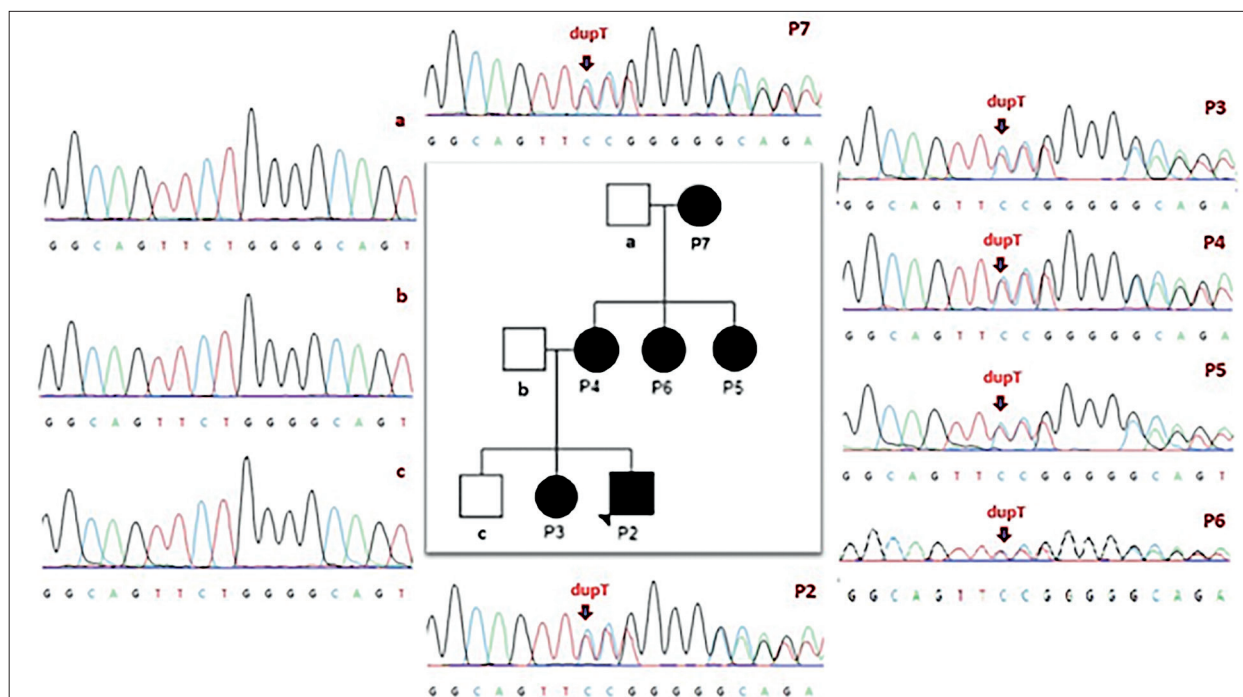


Figure 2. Pedigree of affected family and sanger sequencing data of the *KIF11* gene NM_004523.4: c.2946dup (p.Leu983SerTer6) variant.

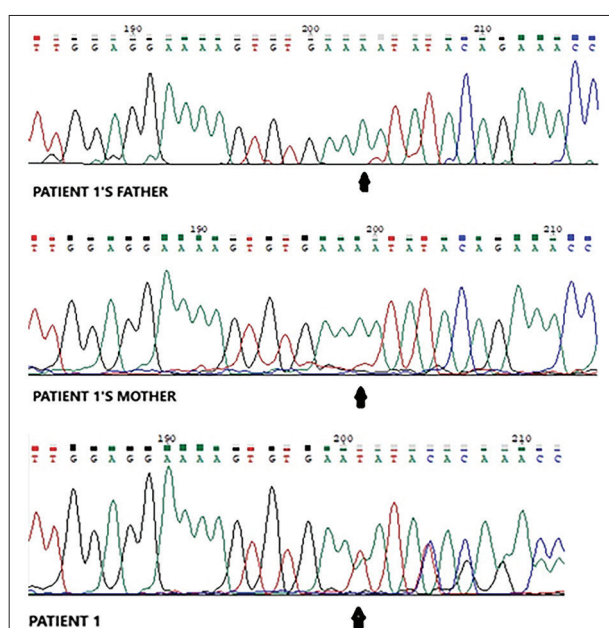


Figure 3. Sanger sequencing chromatograms of Patient 1 and his parents were obtained. Patient 1 carried the NM_004523.4:c.2224_2225del (p.Asn742TyrfsTer6) variant in the *KIF11* gene. This variant was identified as de novo, and no deletion was observed in the sequences of either parent.

grandmother, and two aunts. Although the mother and grandmother did not exhibit lymphedema or visual disturbances, the grandmother demonstrated mild cognitive impairment. The sister had -2.5 diopters of myopia but

lacked cognitive deficits or lymphedema. The affected aunts showed severe cognitive impairment and advanced congenital vision loss, with one aunt also presenting with cataracts and craniosynostosis (Table 1).

DISCUSSION

This study presents two index patients and five family members from different families, all exhibiting the clinical phenotype of MCLMR, in which two distinct novel variants in the *KIF11* gene were identified. The severity of clinical manifestations varies across three generations of affected family members. Variants in the *KIF11* gene have previously been associated with the “Microcephaly with or without Chorioretinopathy, Lymphedema, or Impaired Intellectual Development” phenotype (OMIM: 152950) (<https://www.omim.org/>), which is characterized by the presence of four common features: microcephaly, intellectual disability, lymphedema, and chorioretinopathy. Subsequent studies have also linked variants in the *KIF11* gene to the Familial Exudative Vitreoretinopathy (FEVR) phenotype [8, 10, 15, 16]. Some patients with *KIF11* variants present with isolated FEVR features [2], while others exhibit additional features, including microcephaly, intellectual disability, and lymphedema [1, 8, 9, 17, 18]. This has led to the suggestion that FEVR and MCLMR phenotypes may overlap [8, 9, 17]. The underlying reasons why certain *KIF11* gene variants lead to the MCLMR

phenotype while others result in FEVR remain an area of ongoing investigation.

Ocular anomalies (72%) are among the most common features of the syndrome [5]. Ocular phenotypes in MCLMR patients have been reported to include chorioretinal dysplasia, retinal dystrophy, microphthalmia, nystagmus, myopia, hyperopia, astigmatism, and blindness [1-3, 10, 19-22]. There is significant variability in the ocular phenotype, even among family members carrying the same variant and between the two eyes of an individual [1, 10, 23]. Detailed eye examinations are essential for the early detection of ocular anomalies in patients who present with other features of the syndrome. In this study, Patient 1 exhibited myopia (-10.5), astigmatism (-4.5), along with keratoconus and optic nerve hypoplasia, which have been rarely reported in previous studies (Table 1). In Patient 2, no pathological ocular findings were observed at the age of one, while the patient's sister, who carried the same variant, had -2.5 diopters of myopia. The mother had normal eye findings, while the two maternal aunts experienced congenital severe vision loss, with one of them having a history of cataract surgery (Table 1).

Other features of the syndrome also demonstrate variability across studies. The most common clinical features in MCLMR syndrome, in order of frequency, are microcephaly, ocular anomalies, intellectual disability, and lymphedema. None of these features exhibit full penetrance, and their severity and distribution vary even among patients with the same variant. While the frequencies of these features range from 40% to 75% in different studies, the de novo inheritance rate is high, and incomplete penetrance has been reported in familial patients, with parents carrying the variant showing variability in clinical expression [1, 2, 5, 18].

Microcephaly (91%) is typically congenital and is the most common finding in the syndrome, with its severity ranging from -2 SDS to -9.5 SDS [5]. In the first reported cohort of patients, all patients exhibited microcephaly [1]. However, subsequent studies have reported patients without [2, 5, 18]. In some instances, the degree of microcephaly may be mild, potentially delaying clinical diagnosis. In the present study, the presence of microcephaly in the mother and sister of patient 2 was revealed during genetic analysis (Table 1).

Previous literature has reported that lymphedema occurs in 47% of patients within a cohort of 87 individuals [5]. Lymphedema typically affects the lower extremities and is often detected in the neonatal period. However, a few patients with adult-onset, intermittent lymphedema have also been described [2]. In our study, lymphedema was detected prenatally in patient 2 via ultrasound, prompting referral to the medical genetics' clinic. To our knowledge, this is the first

reported patient of dorsal pedal edema occurring in the prenatal period in MCLMR syndrome patients. No lymphedema was observed in patient 1 or among the family members of patient 2 carrying the same variant (Table 1). This finding is significant as it suggests that *KIF11* gene variants may present with dorsal pedal edema during the prenatal period.

Cognitive functions in patients with MCLMR syndrome range from normal to varying degrees of intellectual disability, from mild to severe. Rarely, neurobehavioral symptoms such as ADHD, sleep disorders, agitation, and autism have been reported [2, 3]. In our patients, Patient 1 received support education due to learning difficulties and also underwent therapy for anger outbursts, showing positive outcomes. The mother and sister of patient 2, both carrying the same variant, exhibited normal intellectual development, while both of the patient's aunts had severe intellectual disability (Table 1).

In addition to the commonly observed features of the syndrome in our study, patient 1 also had a history of seizures, which is less frequently reported in the literature [1, 3, 18]. The seizures were well-controlled with antiepileptic medication (Table 1). Both patient 2 and one of the patient's aunts exhibited signs of craniosynostosis, and patient 2 underwent surgery for this condition (Table 1). Whole exome sequencing (WES) analysis did not identify any significant variants associated with craniosynostosis. To date, craniosynostosis has not been previously reported in MCLMR syndrome, and this finding may represent a novel phenotypic component of the syndrome.

The *KIF11* gene encodes the KIF11 (Eg5) protein, a microtubule motor protein involved in mitosis. Eg5 also plays roles in non-mitotic functions such as endothelial cell proliferation, secretion of protein transport, and protein translation [13, 24, 25]. Over 100 pathogenic/likely pathogenic variants in the *KIF11* gene have been reported, affecting all three functional domains of the KIF11 (Eg5) protein (<https://www.ncbi.nlm.nih.gov/clinvar/>). Most of these variants result in truncated protein formation, and previous studies suggest that this mechanism is linked to "loss of function" and haploinsufficiency [18]. The protein consists of three functional regions: a microtubule-binding motor region, a stalk region, and a tail region [9]. In this study, the two distinct novel variants identified are predicted to result in the loss of the tail domain (p. Asn742TyrfsTer6) and the loss of 67 amino acids in the C-terminal region of KIF11 (p. Leu983SerfsTer6). A review of the literature reveals no significant phenotypic differences between cases with missense and truncating variants [5]. A thorough search of the literature indicates that clinical phenotypes cannot be reliably predicted based solely on the domain or type of variant, suggesting that a clear genotype-phenotype correlation cannot be established.

In this study, we present seven patients from two different families with variants in the *KIF11* gene, demonstrating extreme clinical heterogeneity. This study expands the genotypic and phenotypic spectrum of MCLMR syndrome by introducing novel clinical findings and genetic variants.

DATA AVAILABILITY

The anonymized data analyzed during the current study is available from the corresponding author on reasonable request.

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Written informed consent was obtained from the patients for the publication of their medical case details and any accompanying images.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Ostergaard P, Simpson MA, Mendola A, Vasudevan P, Connell FC, van Impel A, et al. Mutations in *KIF11* cause autosomal-dominant microcephaly variably associated with congenital lymphedema and chorioretinopathy. *Am J Hum Genet*. 2012 Feb 10;90(2):356-62.
- Jones GE, Ostergaard P, Moore AT, Connell FC, Williams D, Quarrell O, et al. Microcephaly with or without chorioretinopathy, lymphoedema, or mental retardation (MCLMR): review of phenotype associated with *KIF11* mutations. *Eur J Hum Genet*. 2014 Jul;22(7):881-7.
- Mirzaa GM, Collins S, Dobyns WB. Corrigendum to "Congenital microcephaly and chorioretinopathy due to de novo heterozygous *KIF11* mutations: Five novel mutations and review of the literature. *Am J Med Genet Part A* 2014 164A:2879-86". *Am J Med Genet A*. 2016 Feb;170(2):547.
- Mears K, Bakall B, Harney LA, Penticoff JA, Stone EM. Autosomal Dominant Microcephaly Associated With Congenital Lymphedema and Chorioretinopathy Due to a Novel Mutation in *KIF11*. *JAMA Ophthalmol*. 2015 Jun;133(6):720-1.
- Schlögel MJ, Mendola A, Fastré E, Vasudevan P, Devriendt K, de Ravel TJ, et al. No evidence of locus heterogeneity in familial microcephaly with or without chorioretinopathy, lymphedema, or mental retardation syndrome. *Orphanet J Rare Dis*. 2015 May 2;10:52.
- Leung AK. Dominantly inherited syndrome of microcephaly and congenital lymphedema. *Clin Genet*. 1985 Jun;27(6):611-2.
- Warburg M, Heuer HE. Chorioretinal dysplasia-microcephaly-mental retardation syndrome. *Am J Med Genet*. 1994 Aug 1;52(1):117.
- Robitaille JM, Gillett RM, LeBlanc MA, Gaston D, Nightingale M, Mackley MP, et al. Phenotypic overlap between familial exudative vitreoretinopathy and microcephaly, lymphedema, and chorioretinal dysplasia caused by *KIF11* mutations. *JAMA Ophthalmol*. 2014 Dec;132(12):1393-9.
- Li JK, Fei P, Li Y, Huang QJ, Zhang Q, Zhang X, et al. Identification of novel *KIF11* mutations in patients with familial exudative vitreoretinopathy and a phenotypic analysis. *Sci Rep*. 2016 May 23;6:26564..
- Wang K, Zhang X, Tian T, Zhao P. Identification of a novel mutation in *KIF11* with functional analysis in a cohort of 516 familial patients with exudative vitreoretinopathy. *Mol Vis*. 2021;27:528-41.
- Ferenz NP, Gable A, Wadsworth P. Mitotic functions of kinesin-5. *Semin Cell Dev Biol*. 2010 May;21(3):255-9.
- Sawin KE, Mitchison TJ. Mutations in the kinesin-like protein Eg5 disrupting localization to the mitotic spindle. *Proc Natl Acad Sci U S A*. 1995 May 9;92(10):4289-93.
- Valentine MT, Fordyce PM, Krzysiak TC, Gilbert SP, Block SM. Individual dimers of the mitotic kinesin motor Eg5 step processively and support substantial loads in vitro. *Nat Cell Biol*. 2006 May;8(5):470-6.
- Song YH, Marx A, Müller J, Woehlke G, Schliwa M, Krebs A, et al. Structure of a fast kinesin: implications for ATPase mechanism and interactions with microtubules. *EMBO J*. 2001 Nov 15;20(22):6213-25.
- Karjosukarso DW, Cremers FPM, van Nouhuys CE, Collin RWJ. Detection and quantification of a *KIF11* mosaicism in a subject presenting familial exudative vitreoretinopathy with microcephaly. *Eur J Hum Genet*. 2018 Dec;26(12):1819-23.

16. Hull S, Arno G, Ostergaard P, Pontikos N, Robson AG, Webster AR, et al. Clinical and Molecular Characterization of Familial Exudative Vitreoretinopathy Associated With Microcephaly. *Am J Ophthalmol*. 2019 Nov;207:87-98.
17. Hu H, Xiao X, Li S, Jia X, Guo X, Zhang Q. KIF11 mutations are a common cause of autosomal dominant familial exudative vitreoretinopathy. *Br J Ophthalmol*. 2016 Feb;100(2):278-83.
18. Birtel J, Gliem M, Mangold E, Tebbe L, Spier I, Müller PL, et al. Novel Insights Into the Phenotypical Spectrum of KIF11-Associated Retinopathy, Including a New Form of Retinal Ciliopathy. *Invest Ophthalmol Vis Sci*. 2017 Aug 1;58(10):3950-9.
19. Atchaneeyasakul LO, Linck L, Weleber RG. Microcephaly with chorioretinal degeneration. *Ophthalmic Genet*. 1998 Mar;19(1):39-48.
20. Hordijk R, Van de Logt F, Houtman WA, Van Essen AJ. Chorioretinal dysplasia-microcephaly-mental retardation syndrome: another family with autosomal dominant inheritance. *Genet Couns*. 1996;7(2):113-22.
21. Jarmas AL, Weaver DD, Ellis FD, Davis A. Microcephaly, microphthalmia, falciform retinal folds, and blindness. A new syndrome. *Am J Dis Child*. 1981 Oct;135(10):930-3.
22. Trzupek KM, Falk RE, Demer JL, Weleber RG. Microcephaly with chorioretinopathy in a brother-sister pair: evidence for germ line mosaicism and further delineation of the ocular phenotype. *Am J Med Genet A*. 2007 Jun 1;143A(11):1218-22.
23. Balikova I, Robson AG, Holder GE, Ostergaard P, Mansour S, Moore AT. Ocular manifestations of microcephaly with or without chorioretinopathy, lymphedema or intellectual disability (MCLID) syndrome associated with mutations in KIF11. *Acta Ophthalmol*. 2016 Feb;94(1):92-8.
24. Bartoli KM, Jakovljevic J, Woolford JL, Saunders WS. Kinesin molecular motor Eg5 functions during polypeptide synthesis. *Mol Biol Cell*. 2011 Sep;22(18):3420-30.
25. Blangy A, Lane HA, d'Hérin P, Harper M, Kress M, Nigg EA. Phosphorylation by p34cdc2 regulates spindle association of human Eg5, a kinesin-related motor essential for bipolar spindle formation in vivo. *Cell*. 1995 Dec 29;83(7):1159-69.